1.目的 Purpose

本標準作業程序主要說明已通過審查之計畫通報試驗偏差，以及計畫主持人未遵照審查通過之計畫書、國內/國際研究倫理相關規範或本本委員會規定進行試驗時的處理作業準則。

The SOP primarily indicates the operational guidelines when handling study deviation occurred in the approved studies, and the PI fails to comply with study protocols, national/international research ethics regulations or KMUHIRB regulations when implementing studies.

2. 適用範圍 Scope

本作業準則適用於本委員會審查通過之試驗計畫，經主動通報、稽核或申訴/投訴之不遵從事件之處理。

This SOP is applicable to the handling of the study protocol approved by the IRB, which generates non-compliance events that are actively reported, audited or filed complaints/appeals.

3.參考文件 References

3.1 人體研究法 (2011 年 12 月)

Human Subjects Research Act (December 2011)

3.2 人體試驗管理辦法 (2009 年 12 月)

Regulations on Human Trials (December 2009)

3.3 藥品優良臨床試驗準則 (2014 年 10 月)

Guidelines of Good Clinical Practice (October 2014)

3.4 醫療器材優良臨床試驗基準 (2014 年 8 月)

Guidelines of Good Clinical Practice for Medical Devices (August 2014)

3.5 赫爾辛基宣言(Declaration of Helsinki) 2013 年中文版，2013

Declaration of Helsinki, Chinese Version, 2013

3.6 人體研究倫理審查本委員會組織及運作管理辦法(衛署醫字第 1010265129 號令)，17 August, 2012

Regulations Governing the Organization and Operational Management of the Institutional Review Board for Human Subject Research (Wei-Shu-Yi-Zi No. 1010265129) (17 August 2012)

3.7 藥品優良臨床試驗準則(衛生福利部部授食字第 1031203335 號令修正發布第 2 條條文)，23 October, 2014

Guidelines of Good Clinical Practice (MOHW Bu-Shou-Shi-Zi No. 1031203335 Amendment Article 2), 23 October, 2014

3.8 WHO Operational Guidelines for Ethics Committees that Review Biomedical Research，WHO 2000

3.9 Forum for Ethical Review Committees in Asia and the Western Pacific，August 2003

3.10 倫理審查本委員會得簡易程序審查之人體研究案件範圍(衛署醫字第 1010265098C 號)，5 July, 2012

The Scope of Human Trial for IRB Expedited Review (Wei-Shu-Yi-Zi No. 1010265098C), 5 July, 2012

3.11 醫療法，(總統華總一義字第 10300013681 號令修正公布第 24、106 條條文)，29 January, 2014

Medical Care Act (President Hua-Zong-Yi-Yi-Zi No. 10300013681 Amendment Article 24, 106), 29 January, 2014

3.12 人體試驗管理辦法(衛署醫字第 0980263557 號公告)，14 December 2009

Regulations on Human Trials (Wei-Shu-Yi-Zi No. 0980263557), 14 December 2009

3.13 人體研究法(總統華總一義字第 10000291401 號令)，18 December 2011

Human Subjects Research Act (President Hua-Zong-Yi-Yi-Zi No. 10000291401), 18 December 2011

3.14 得免取得研究對象同意之人體研究案件範圍(衛署醫字第 1010265083C 號)，5 July, 2012

The scope of human trial waiver of subject consent (Wei-Shu-Yi-Zi No. 1010265083C), 5 July, 2012

3.15 得免倫理審查本委員會審查之人體研究案件範圍(衛署醫字第 1010265079 號)，5 July, 2012

The scope of human trial waiver of IRB review (Wei-Shu-Yi-Zi No. 1010265079), 5 July, 2012

3.16 AAHRPP 基準 Domain I,Element 1.5.D (January 1, 2015)

AAHRPP Standard Domain I, Element 1.5.D (January 1, 2015)

4.名詞定義 Terminology

4.1 不遵從事件(non-compliance)：未能遵照本委員會所核准之計畫執行人體研究及試驗計畫案、臨床試驗相關法規或本院相關規範。違規情節有不同的等級，從輕微至重大、僅發生一次或是發生好幾次。可由計劃主持人及試驗委託者於執行中，或由本委員會定期評估時，發現未依照本委員會核准之計畫內容執行時通報。包括輕微不遵從事件(minor non-compliance)、嚴重不遵從事件(Serious non-compliance) 、持續性不遵

從事件(Continuing non-compliance) 。

Non-compliance: the event that does not comply with the human study and study protocol approved by the IRB, clinical trial-related laws and provisions or KMUHIRB regulations. The violation can be classified in several levels, from mild to serious, once or repeatedly. The PI and sponsor may uncover such event during study implementation, or the IRB may uncover such event during regular evaluation, and report promptly due to the failure of complying with the approved study protocol. Such event includes minor non-compliance, serious non-compliance, and continuing non-compliance.

4.2 輕微不遵從事件：又稱為試驗偏差(Protocol Deviation)，不遵從事件不影響研究原先預估之風險與利益、受試者安全性及繼續參與研究之意願。

Minor non-compliance: which also called “protocol deviation”. It is a non-compliance event that will not affect the original estimated risks and benefits of the study, the safety of the subject and the subject’s willingness to continue participating in the study.

4.3 嚴重不遵從事件：又稱為試驗違規(Protocol Violation)，不遵從事件影響研究原先預估之風險與利益、受試者安全性及繼續參與研究之意願。

Serious non-compliance: which is also called “protocol violation”. It is a non-compliance event that will affect the original estimated risks and benefits of the study, the safety of the subject and the subject’s willingness to continue participating in the study.

4.4 持續性不遵從事件：不遵從事件若不採取適當措施，可能會持續出現偏差或違規。

Continuing non-compliance: non-compliance events that may become deviation or violation if no proper measures have been adopted.

5.作業內容 Scope of operation

5.1 流程 Process

程序 Procedure	**權責 Rights and responsibilities**	**相關文件 Related documents**
通報 Report	本委員會/試驗相關人員/臨床試驗管理委員會 IRB/Study-related personnel/CTMC	試驗偏差報告/改善表 Study deviation report/Improvement form 不遵從事件通報表 Non-compliance event report form 臨床試驗計畫稽核結果/缺失項目 Clinical trial audit results/Defect items
行政審查 Administrative review	行政人員 Administrative staff	通報文件 Report files
事件調查 Event investigation	執行祕書 Executive secretory 委員/專家 Member/Experts	通報文件 Report files
本委員會共識/決議 IRB consensus/Resolution	本委員會 IRB	會議記錄 Meeting minutes
追蹤改善與稽核 Improve and audit follow-up	計畫主持人 Principal Investigator 臨床試驗管理本委員會 CTMC	試驗偏差報告/改善表 Study deviation report/Improvement form
審查/稽核結果通知 Review/Audit results notification	本委員會 IRB	試驗偏差審查決議通知書 Study deviation review resolution notification
紀錄保存 Retain records	行政人員 Administrative staff	會議記錄 Meeting minutes

5.2 職責 Responsibilities

5.2.1 試驗計畫主持人、協同主持人、研究人員、臨床研究專員及研究贊助廠商：當獲知不遵從事件發生時，計畫主持人應於 15 個工作日內通報本委員會，並於通報後 7 個工作日內將不遵從 (試驗偏差/違規) 事件通報表，提交本委員會、試驗委託者；經主管機關核准進行之臨床試驗，應同時提交主管機關。

PI, co-investigator, research personnel, CRA and Sponsor: The PI shall report the event to the IRB within 15 working days after being aware of the non-compliance event, and submit the non-compliance (study deviation/violation) event notification form to the IRB and sponsor within 7 working days after the report. The competent authority-approved clinical study shall be submitted to the competent authority at the same time.

5.2.2 臨床試驗管理委員會(CTMC)：定期稽核及追蹤本委員會審核通過之一般及特殊/易受傷害族群等計畫案，或本委員會函請進行稽核之計畫案，並將稽核/追蹤結果書面資料回報本委員會。

CTMC: is to regularly audit and follow up KMUHIRB-approved regular studies or studies involving special/vulnerable population. Or the IRB will issue a letter to ask the CTMC conducting the audit and send back the audit/follow-up results in writing to the IRB.

5.2.3 執行秘書、委員/專家：審查會議前，應對不遵從事件進行調查，必要時執行祕書得邀請計畫主持人列席報告。

Executive secretary, member/experts: They shall conduct inspections on

the non-compliance event before the meeting, and ask the PI to attend the meeting for report if necessary.

5.2.4 行政人員：行政審查通報文件之完整性。將本委員會審查核定結果彙整成書面資料，並通知計畫主持人及試驗委託者。

Administrative staff: to maintain the completeness of the administrative review report files. The administrative staff will summarize the review results, establish written documents and inform the PI and the sponsor.

5.3 不遵從事件處理流程

The process of handling non-compliance events

5.3.1 通報 Report

5.3.1.1 凡在試驗執行期間發現任何未依本委員會核准之計畫內容、臨床試驗相關法規或本院相關規範時，計畫主持人應依規定通知試驗委託者及本委員會，並提供詳細書面資料說明不遵從情形、原因、後續處理及日後改善措施之內容。

If any events are found non-complaint to the study protocol, clinical trial-related laws and provisions or the regulations of KMUH during the implementation of the study, the PI shall inform the sponsor and KMUHIRB by law and provide detailed written files to describe the situations, reasons, subsequent management and improvement measure of the non-compliance event.

A.計畫主持人通報不遵從事件時應檢附下列資料：

The PI shall submit the following files while reporting non-compliance events:

(A) 公文或其相關文件

Official letters or relevant files

(B) 不遵從(試驗偏差/違規)事件通報表

Non-compliance (study deviation/violation) report form

5.3.1.2 本委員會於定期審查計畫案之期中/結案報告、接獲申訴/投訴時，發現有不遵從事件疑慮時，應於行政會議中提請臨床試驗管理委員會進行稽核。

If the IRB have uncovered or raised concerns about non-compliance events during regular review of study interim/final reports or receiving complaints/appeals, the IRB shall ask the CTMC to conduct audit during the administrative meeting.

5.3.2 行政審查 Administrative review

5.3.2.1 行政人員於 1 個工作天檢視不遵從事件通報應檢附之資料(含電子檔)，文件不齊全者，通知補件。

The administrative staff will review all materials required for reviewing non-compliance events within 1 working day (including the electronic files). For those submitted incomplete materials, the IRB will inform the applicant to supply missing files.

5.3.2.2 資料齊全後轉知執行祕書。

After confirming that all materials are well-prepared, they will be transferred to the executive secretary.

5.3.3 事件調查 Even inspection

5.3.3.1 執行祕書進行調查，必要時可會同委員/專家進行實地訪查。

The executive secretary will conduct the inspection, and the members/experts may be invited to join the site visit if necessary.

5.3.3.2 調查結果提交審查會進行決議。

The inspection review will be submitted to the meeting for resolutions.

5.3.4 審查會議 Review meeting

5.3.4.1 本委員會經討論後決議事件之處理。

The handling of the IRB after discussion and making the resolutions.

A.輕微且不持續事件

For mild and incontinuous events

(A)「存查，同意試驗繼續進行」：會議討論後，做成紀錄、存檔備查，必要時邀請計畫主持人於審查會列席說明後再決議。

"Retain for reference and approve for the continuance of the study implementation": Form a record and retain for reference after the meeting. Invite the PI to attend the meeting for descriptions if necessary, and then make the decision.

a. 繼續追蹤監測

Continue follow-up monitoring

b. 主持人及相關人員須接受再教育課程

The PI or relevant personnel shall receive re-training programs.

c. 須依審查本委員會建議修正，並接受後續追蹤監測或查核。

Amend the file based on the IRB review comments and receive subsequent follow-up monitoring or inspection.

(B)「實地訪視」：不遵從事件可能影響後續執行研究時受試者之安全疑慮時，本委員會得進行訪視。

"Site visit": If the non-compliance event may raise concerns about the safety of the subject in the future, the IRB may conduct a site visit.

B.嚴重或持續事件

For serious or continuous events

IRB 委員考慮措施 (包括但不侷限於以下)：

The IRB members may consider using some measures (including but not limited to) as follows:

(A) 必要處置（Required）

Required managements

a. 繼續進行該試驗並繼續追蹤監測

Continue implementing the study and continue follow-up and monitoring

b. 暫停該計畫進行，直到改善計畫通過審查會審查。

Suspend the study until the improvement plan has been reviewed and approved by the IRB.

c. 終止該計畫進行

Terminate the study

(B) 額外處置（Optional）

Optional managements

a. 修改計畫書、受試者同意書。

Amend study protocols and subject ICF.

b. 在受試者同意過程中揭露相關資訊。

Disclose relevant information during the process of obtaining the informed consent.

c. 提供資訊給已完成計畫的受試者。

Provide information to subjects who have completed the study procedures.

d. 要求計畫參與中的受試者重新簽署同意書。

Ask the participating subjects to sign the ICF again.

e. 修改持續審查頻率。

Amend the frequency of continuing review.

f. 通知委託機構加強監測。

Inform the CRO to reinforce monitoring.

g. 監測受試者同意過程。

Monitoring the process of obtaining informed consent.

h. 獲得更多資訊後再做最後決議。可能影響研究後續受試者之安全時，本委員會得進行實地訪視，以決定試驗是否繼續進行。

Make the final resolution after obtaining more information. If it may affect the subsequent safety of the subject, the IRB may conduct a site visit to decide whether the study could be continued.

i. 轉知相關單位（如：受試者保護中心、法規單位、行政管理中心）。

Inform relevant units (e.g. CHSP, law enforcement units, administrative center, etc.)

j. 計畫主持人、研究團隊須接受再教育訓練__小時。

The PI or research team shall receive re-training for __ hours.

k. 限制研究結果發表。

The publication of the study results is restricted.

l. 不受理計劃主持人申請新案，不受理期限為 ___ 個月。

No new applications of the PI will be received for ___ months.

m. 相關訊息通知計畫參與中的受試者(若該資訊會影響受試者是否繼續參與計畫)。

Inform participated subjects about relevant information (if the information may affect the subject's willingness to decide whether or not to continue participating in the study)

5.3.4 通知計畫主持人 Informing the PI

5.3.4.1 行政人員應於會議結束後 10 個工作天內，以不遵從(含試驗偏差/違規) 事件審查結果通知表通知計畫主持人。

The administrative staff shall inform the PI about the non-compliance (including study deviation/violation) review results notification form within 10 working days after the meeting is finished.

5.3.4.2 若會議決議為「計畫暫停」或「計畫終止」或「不受理計劃主持人申請新案」，計畫主持人如有異議，得於 14 個工作天內以書面向本委員會提出申覆，否則案件將依會議決議進行處理。

If the meeting resolution is “suspend the study” or “terminate the study” or “no new application from the PI will be received”, and the PI holds opinions against the resolution, the PI may apply for appeal to the IRB within 14 working days, otherwise the case will be processed as the meeting resolution.

5.3.5 歸檔 Archiving

5.3.5.1 不遵從(含試驗偏差/違規)事件通報表、不遵從(含試驗偏差/違規)事件審查結果通知表、不遵從事件審查意見回覆表，應歸檔管理。

Non-compliance (including study deviation/violation) report form, review results notification form for non-compliance (including study deviation/violation), and the reply to non-compliance review comments shall be archived for management.

6.附件 Attachment

6.1 附件一 (KMUH/IRB/AF/3.4-01/11.0)不遵從(含試驗偏差/違規)事件通報表

Attachment 1 (KMUH/IRB/AF/3.4-01/11.0) Non-compliance (Including Study Deviation/Violation) Report Form

6.2 附件二 (KMUH/IRB/AF/3.4-02/11.0)不遵從(含試驗偏差/違規)事件審查結果通知表

Attachment 2 (KMUH/IRB/AF/3.4-02/11.0) The Review Results Notification Form for Non-Compliance (Including Study Deviations/Violations)

6.3 附件三 (KMUH/IRB/AF/3.4-03/11.0)不遵從(含試驗偏差/違規)事件審查意見回覆表

Attachment 3 (KMUH/IRB/AF/3.4-03/11.0) Reply to the Non-Compliance (Including Study Deviation/Violation) Review Comments